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10/597,290	12/30/2008	Robert James Nash	2245.074	8876

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EXAMINER	
BASQUILL, SEAN M	

ART UNIT	PAPER NUMBER
1613	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,290	NASH ET AL.	
	Examiner	Art Unit	
	SEAN BASQUILL	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88,94 and 96-113* is/are pending in the application.

4a) Of the above claim(s) *96-107 and 110-113* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88,94,108 and 109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 88 and 94 have been amended, and Claims 1-87, 89-93 and 95 cancelled. Claims 96-107 remain withdrawn as directed to a non-elected invention. Claims 108-113 haven been newly added, with Claims 110-113 being withdrawn as directed to a nonelected invention. Claims 88, 94, 108, and 109 are presented for examination.

Previous Rejections

2. Applicants' arguments, filed 15 March 2011, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 First Paragraph – NEW MATTER

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 88, 94, 108, and 109 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. Specifically, the examiner cannot in the entirety of applicants disclosure identify a disclosure of either a vaccine composition or methods of vaccination utilizing the combination of a polyhydroxylated pyrrolizidine alkaloid such as casuarine, a neoantigen, and a TLR ligand. This is a new matter rejection.

The description requirement of the patent statute requires a description of an actual invention, not merely an indication of a result that one might achieve if one made that invention. See, e.g., In re Wilder, 22 USPQ 369, 372-3 (Fed. Cir. 1984) (holding that a claim was not adequately described because the specification did 'little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate'). This matter is of particular importance in the evaluation of claims drawn to a chemical genus which identifies a core compound bearing variable substituents. It has been held that "a generic claim may define the boundaries of a vast genus of chemical compounds, and yet the question may still remain whether the specification...demonstrates that the applicant has invented species sufficient to support a claim to a genus" with such breadth. Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co., 94 USPQ2D 1161, 1171 (Fed. Cir. 2010). An adequate written description requires a precise definition, such as by structure, formula, chemical name, physical properties, or other properties of species falling within the genus sufficient to distinguish the genus from other materials. Id., quoting Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997).

However, merely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species. Ariad, 94 USPQ2D at 1171. 35 U.S. C. 112,

first paragraph, requires a description of the invention that "clearly allow[s] persons of ordinary skill in the art to recognize that the inventor invented what is claimed." Ariad at 1172, quoting Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555 (1562-63) (Fed. Cir. 1991) (emphasis added). A sufficient disclosure is one which reasonably conveys to one having ordinary skill in the art that the inventor had possession of the claimed subject matter as of the filing date of the application in question. Vas-Cath, 935 F.2d at 1563. The description must reasonably describe the invention, not simply indicate a result which one might achieve if one actually made the invention. Eli Lilly, 119 F.3d at 1568. It is critical to remember that "patents are not awarded for academic theories, no mater how groundbreaking or necessary to the later patentable inventions of others. '[A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.'" Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co., 94 USPQ2D 1161, 1173-74 (Fed. Cir. 2010), quoting University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 930 (Fed. Cir. 2004). Requiring a written description of the invention limits patent protection to those who actually perform the difficult work of "invention" – that is, conceive of the complete and final invention with all its claimed limitations – and disclose the fruits of that effort to the public. Id.

Here, applicants have claimed the use of a combination of polyhydroxylated pyrrolizidine alkaloid, neoantigen, and TLR ligand in vaccinating subjects in need of such treatment. In reviewing the applicants disclosure as originally filed, the examiner can find no previous mention of such a combination, and aside from the previous set of claims presented as of the original filing date of the instant application, can find no mention of the use of TLR ligands except as a part of a dendrite cell maturation medium. While independent and discrete portions

of the disclosure may certainly contain the individual elements of the invention presently claimed, it is critical to remember that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention. Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1567 (Fed. Cir. 1997).

The skilled artisan, in reviewing the disclosure as originally filed, would not conclude that the invention claimed was sufficiently supported as required by the first paragraph of 35 U.S.C. 112. As such, the invention put forth in instant Claims 88, 94, 108, and 109 do not find support as required by Ariad in the disclosure as originally filed.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 88, 94, 108, and 109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shizuo Akira, Mammalian Toll-Like Receptors, 15 CURR. OPIN. IMMUNOL. 5, 8, 9 (February 2003) ("Akira"), in view of Ruain Xu, et al, Molecular Therapeutics of HBV, 3 CURR. GENE THERAPY 341 (2003) ("Xu"), Alison Watson, et al, Polyhydroxylated Alkaloids - Natural Occurrence and Therapeutic Applications, 56 PHYTOCHEM. 265 (2001) ("Watson"), as evidenced by Andrew Bell, et al, Synthesis of Casuarines [Pentahydroxylated Pyrrolizidines] by Sodium Hydrogen Telluride-Induced Cyclisations of Azidodimesylates, 38 TET. LET. 5869 (1997) ("Bell"), as put froth in the previous office action, and further in view of Guity Ghaffari, et al, Human Lymphocyte Proliferation Responses Following Primary Immunization with Rabies Vaccine as Neoantigen, 8 CLIN. DIAG. LAB. IMMUNOL. 880 (2001) (hereinafter "Ghaffari').

Applicants amendment of the pending claims to recite a method of vaccination using a combination of polyhydroxylated pyrrolizidine alkaloid such as casuarine, a neoantigen, and a TLR ligand requires analysis to accurately determine the metes and bounds of the subject matter encompassed by the instant claims. In particular, applicants have defined "neoantigen" as "any newly expressed antigenic determinant," (Spec. page 20), as well as tumor associated, and virally, bacterially, or protozoally expressed antigens. (Claim 109). The examiner therefore considers the term "neoantigen" as encompassing any antigen newly expressed as a result of exposure to tumor, bacterial, o4r protozoa cells, or as a result of viral infection.

Akira, Xu, Watson, and Bell, discussed previously, suggests the reasoning behind as well as the value to be obtained by the combined immunotherapy of a polyhydroxylated pyrrolizidine alkaloid such as casuarine when combined with a toll-like receptor ligand in terms of amplifying innate immune responses, but does not address the introduction of a neoantigen as part of the therapy.

However, Ghaffari discusses vaccination with the rabies virus serving as a neoantigen, as well as assessing immune responses in patients so vaccinated. (Pg. 880). Ghaffari therefore describes the use of rabies vaccine, particularly a viral rabies vaccine, as a neoantigen promoting an innate immune response in the course of immunization. (Pg. 883). Not only does the rabies vaccine disclosed by Ghaffari fit the definition of "neoantigen" as put forth in the instant specification and claims, but the virus vaccine is itself independently recognized as a viral neoantigen when administered to patients not previously exposed to the virus. (Pg. 880). Ghaffari therefore discloses the use of viral rabies vaccine as a neoantigen for the vaccination of individuals against rabies infection.

Taken in combination with the teachings of Akira, Xu, Watson, and Bell discussed previously, the skilled artisan as of the time of the instant invention would not only be aware of vaccination using viral rabies vaccine as a neoantigen to promote an innate immune response against the rabies virus., as well as the value of immunostimulation to promote development of innate immunity by administering a combination of a polyhydroxylated pyrrolizidine alkaloid such as casuarine and a toll-like receptor ligand. Such a combination amounts to little more than following the suggestion of the combined teaching of the art, with each element operating as the skilled artisan would expect.

Applicants arguments, directed as they were to the lack of neoantigen disclosed by the previous rejections, are moot in light of the instant rejection addressing those limitations.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 88, 94, 108 and 109 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 43-60, 61, and 62 of copending Application No. 10/597,296 in view of Akira and Ghaffari as described above. The '296 application claims methods of polarizing an immune response by administering a combination of an antigen and an alkaloid such as the casuarines of the instant claims, but does not indicate a toll-like receptor ligand and neoantigen can be co-administered. However, by the teaching of Akira, TLR ligands such as lipopolysaccharides are well-known as antigens suitable for promoting an immune response in the development of innate immunity, and therefore would have been known as a suitable immune polarizing antigen to the skilled artisan at the time of the instant invention, particularly when administered in combination with a neoantigen such as the rabies virus vaccine taught by Ghaffari.

This is a provisional obviousness-type double patenting rejection.

Applicants arguments, directed as they were to the lack of neoantigen disclosed by the previous rejections, are moot in light of the instant rejection addressing those limitations.

6. Claims 88, 94, 108 and 109 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 64-74 of copending Application No. 10/543,014 in view of Akira and Ghaffari as described above. The '014 application claims methods of treating a disease such as a viral or bacterial infection by administering at least an alkaloid such as the casuarines of the instant claims, but does not indicate a toll-like receptor ligand and neoantigen can be co-administered. However, by the teaching of Akira, TLR ligands such as lipopolysaccharides are well-known as antigens suitable for promoting an immune response in the development of innate immunity to viruses and bacteria, and therefore would have been known as a suitable means of treating such diseases by the skilled artisan at the time of the instant invention, particularly when administered in combination with a neoantigen such as the rabies virus vaccine taught by Ghaffari.

This is a provisional obviousness-type double patenting rejection.

Applicants arguments, directed as they were to the lack of neoantigen disclosed by the previous rejections, are moot in light of the instant rejection addressing those limitations.

Conclusion

No Claims stand allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN BASQUILL whose telephone number is (571)270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Kwon can be reached on (571) 272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KARLHEINZ R SKOWRONEK/
Primary Examiner, Art Unit 1631

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